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**A LOW, RATHER THAN A HIGH, TOTAL PLASMA HOMOCYSTEINE IS AN INDICATOR OF POOR OUTCOME IN HEMODIALYSIS PATIENTS.** K. Kalantar-Zadeh, G. Block,

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An increased level of total plasma homocysteine (tHcy) is a risk factor of poor cardiovascular outcome in the general population. However, a decreased, rather than an increased, tHcy concentration may predict poor outcome in MHD patients, a phenomenon referred to as risk factor paradox or reversal. We examined associations between tHcy level and markers of malnutrition-inflammation complex syndrome and 12-month prospective hospitalization and mortality in 367 MHD patients, aged  $54.5 \pm 14.7$  (mean  $\pm$  SD) years, who included 199 men and 55% diabetics. tHcy was  $24.4 \pm 11.8$   $\mu\text{mol/L}$ , and 94% of the patients had hyperhomocysteinemia (tHcy  $> 13.5$   $\mu\text{mol/L}$ ). tHcy had weak to moderate but statistically significant bivariate and multivariate correlations with some laboratory markers of nutrition (serum albumin, prealbumin, creatinine, and urea nitrogen) but no significant correlation with serum C-reactive protein or two pro-inflammatory cytokines (interleukin 6 and tumor necrosis factor alpha). During 12 months of follow-up, 191 MHD patients were hospitalized, 37 died, 9 underwent renal transplantation, and 38 transferred out. Hospitalization rates were significantly higher in patients with lower tHcy levels. Mortality rate in the lowest tHcy quartile (17.4%) was significantly higher compared to other three quartiles

(6.5 to 9.8%, Kaplan-Meier  $p=0.04$ ). Relative risk of death for the lowest tHcy quartile, even after adjustment for case-mix and serum albumin, was 2.27 (95% confidence interval: 1.14-4.53,  $p=0.02$ ). Hence, tHcy may be a more exclusive nutritional marker in MHD patients with no association with inflammatory measures. Despite a very high prevalence of hyper-homocysteinemia in MHD patients, lower values of tHcy are paradoxically associated with increased hospitalization and mortality. The lowest tHcy quartile confers a 2-fold increase in risk of death independent of hypoalbuminemia. The nutritional feature of tHcy in MHD patients may explain its reverse association with outcome.